



USSN: 09/528,682  
Atty. Dkt. No.: PP000342.0105  
2302-0342.10

**PATENT**

**CERTIFICATE OF MAILING PURSUANT TO 37 CFR § 1.8**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on August 22, 2005.

8/22/05  
Date

Michelle Hobson  
Signature

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In Re Application of:

PIZZA et al.

Serial No.: 09/528,682

Filing Date: March 20, 2000

Title: IMMUNOGENIC DETOXIFIED MUTANT  
E. COLI LT-A TOXIN

Examiner: M. Borin

Group Art Unit: 1631

Confirmation No.: 5794

**INFORMATION DISCLOSURE STATEMENT  
UNDER 37 C.F.R. §1.97(b)**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sirs:

In accordance with the duty of disclosure set forth in 37 C.F.R. §1.56, Applicant(s) hereby submits the following information in conformance with 37 C.F.R. §§1.97 and 1.98.

- Pursuant to 37 C.F.R. §1.98, copies A1, B1 - B7 and C1 – C29 cited in the attached Form PTO/SB/08 are enclosed.
- No copy of the U.S. publication \_\_\_\_\_ listed on the attached Form PTO/SB/08A are being provided because the Office waives the requirement under 37 C.F.R. 1.98 (a) (2) (i) for submitting a copy of each cited U.S. patent and each U. S. patent application publication for all U.S. national patent applications filed after June 30, 2003
- No copies of the publications listed on the attached Form PTO/SB/08A are being provided pursuant to 37 C.F.R. §1.98(d) because the publications were previously cited by or submitted to the Office in prior Application

Serial No. \_\_\_\_\_ to which the above-identified application claims priority under 35 U.S.C. §120.

- Publication(s) \_\_\_\_\_ listed on the attached Form PTO/SB/08A were cited in a foreign search or examination report corresponding to PCT application serial no. \_\_\_\_\_ and mailed on \_\_\_\_\_.
- Enclosed is a copy of a non-English publication(s) \_\_\_. Pursuant to §609 of the M.P.E.P., Applicant submits the attached foreign search or examination report, which cites such non-English language publication(s).
- Enclosed is a copy of a non-English publication(s) \_\_\_. English language publication \_\_ (copy enclosed) claims priority from this non-English publication.
- Enclosed is an explanation of non-English publication(s) \_\_ for which an English translation is not available.
- Enclosed is an English translation of non-English publication(s) \_\_ cited in the attached Form PTO/SB/08A.
- Enclosed is a copy of pending patent Application Serial No. \_\_\_\_.

This Information Disclosure Statement is filed within any one of the following time periods:

- within three months from the filing date of this national application other than a CPA under 37 C.F.R. § 1.53(d);
- within three months from the date of entry of the national stage as set forth in 37 C.F.R. §1.491 in this international application;
- before the mailing date of a first office action on the merits; or
- before the mailing of a first office action after the filing of a request for continued examination under 37 C.F.R. §1.114.

This Information Disclosure Statement under 37 CFR § 1.97 is not to be construed as a representation that: (i) a complete search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the information, protocols, results and the like reported by third parties are accurate or enabling; or (iv) the above information constitutes prior art to the subject invention.

It is respectfully requested that the Examiner consider the above-noted information and return an initialed copy of the attached Form PTO/SB/08A to the undersigned.

Respectfully submitted,

Date: August 22, 2005

By: D. Pasternak  
Dahna S. Pasternak  
Registration No. 41,411

CHIRON CORPORATION  
Intellectual Property – R440  
P.O. Box 8097  
Emeryville CA 94662-8097  
Tel: (510) 655-8730  
Fax: (510) 655-3541

A rectangular stamp with rounded corners. The text 'AUG 24 2005' is stamped diagonally across the center. In the bottom left corner, there is a small 'P-1'. In the bottom right corner, the word 'OFFICE' is partially visible, and above it, '110' is stamped. The stamp has a thin black border.

PTO/SB/08A (08-00)

<p>Substitute for form 1449 (PTO-1050)</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b></p> <p><i>(use as many sheets as necessary)</i></p>				<p><i>Complete if Known</i></p>	
Sheet	1	of	3	Application Number	09/528,682
				Filing Date	March 20, 2000
				First Named Inventor	PIZZA et al.
				Group Art Unit	1631
				Examiner Name	M. Borin
				Attorney Docket Number	PP000342.0105

## **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

of

3

*Complete if Known*

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<b>Attorney Docket Number</b>	PP000342.0105

U.S. PATENT DOCUMENTS

## FOREIGN PATENT DOCUMENTS

Examiner Signature		Date Considered	
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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number.

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<sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

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Sheet	2	of	3	Attorney Docket Number	PP000342.0105 (2300-0342.10)

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			
	C1	Burnette, "The Advent of Recombinant Pertussis Vaccines." <i>Biotechnol.</i> 8:1002-1005 (1990)			
	C2	Burnette, <i>Vaccine Research &amp; Developments</i> Chapter 6, Marcel Dekker Inc., New York, New York (1992)			
	C3	Communication to EPO Concerning Replacement Claims for Filing with the EPO in Application No. 99922284.7 (2003)			
	C4	de Haan, et al., "Mutational Analysis of the Role of ADP-Ribosylation Activity in the Adjuvant Properties of the Escherichia Coli Heat-Labile Enterotoxin Towards Intranasally Administered Keyhole Limpet Hemocyanin." <i>Eur. J. Immunol.</i> 28:1243-1250 (1998)			
	C5	Del Guidice, et al., "Genetically Derived Toxoids for use as Vaccines and Adjuvants." <i>Vaccine</i> 17:S44-S52 (1999)			
	C6	Dickinson & Clements, "Dissociation of Escherichia coli heat-labile enterotoxin adjuvanticity from ADP-ribosyltransferase activity", <i>Infect. Immun.</i> , 63:1617-1623 (1995)			
	C7	EPO Communication pursuant to Article 96(2) EPC relating to Application EP No. 94928455.8-2116 (2001)			
	C8	"Multicomponent Vaccine Development." <i>NIH Guide</i> Volume 22, Number 28 (1993)			
	C9	Green, Bruce, Curriculum Vitae			
	C10	Grant et al., "Role of trypsin-like cleavage at arginine 192 in the enzymatic and cytotoxic activities of Escherichia coli heat-labile enterotoxin", <i>Infect. Immun.</i> , 62:4270-4278 (1994).			
	C11	Hagen, Michael, Curriculum Vitae			
	C12	Hagiwar, et al., Effectiveness and Safety of Mutant Escherichia Coli Heat-Labile Enterotoxin (LT H44A) as an Adjuvant for Nasal Influenza Vaccine." <i>Vaccine</i> 19:2071-2079 (2001)			
	C13	Hartman, et al., "Native and Mutant Forms of Cholera Toxin and Heat-Labile Enterotoxin Effectively Enhance Protective Efficacy of Live Attenuated and Heat-Killed Shigella Vaccines." <i>Infect. Immun.</i> 67:5841-5847 (1999)			
	C14	Hazama, et al., "Intranasal Immunization Against Herpes Simplex Virus Infection by using a Recombinant Glycoprotein D Fused with Immunomodulating Proteins, the B Subunit of Escherichia Coli Heat-Labile Enterotoxin and Interleukin-2." <i>Immunology</i> 78:643-649 (1993)			
	C15	Hirst, et al., "Cholera Toxin and Related Enterotoxins as Potent Immune Modulators." <i>J. Appl. Microb. Symp. Suppl.</i> 48:26S-34S (1998)			
	C16	Hirst, <i>The Comprehensive Sourcebook of Bacterial Protein Toxins</i> , Chapter 6, Academic Press, pgs. 104-130, (1999)			
	C17	Lobet et al., "Effect of site-directed mutagenic alterations on ADP-ribosyltransferase activity of the A subunit of Escherichia coli heat-labile enterotoxin", <i>Infect. Immun.</i> 59:2870-2879 (1991)			
	C18	Lycke, et al., "Strong Adjuvant Properties of Cholera Toxin on Gut Mucosal Immune Responses to Orally Presented Antigens." <i>Immunol.</i> 56:301-308 (1986)			
	C19	Lycke, et al., "The Mechanism of Cholera Toxin Adjuvanticity." <i>Res. Immunol.</i> 198:504-520 (1997)			
	C20	Martindale, <i>Royal Pharmaceutical Society of Britain</i> Pharmaceutical Press, London, England, pgs.1277-1304(1993)			
	C21	Rappouli, et al., "Structure and Mucosal Adjuvanticity of Cholera and Escherichia Coli Heat-Labile Enterotoxins." <i>Immunol. Today</i> 20:493-500 (1999)			
	C22	Spangler, "Structure and Function of Cholera Toxin and The Related Escherichia Coli Heat-Labile Enterotoxin." <i>Microbiol. Rev.</i> 56:622-647 (1992)			
	C23	Streatfield, et al., "Intermolecular Interactions Between the A and B Subunits of Heat-Labile Enterotoxin from Escherichia Coli Promote Holotoxin Assembly and Stability In Vivo." <i>PNAS USA</i> 89:12140-12144 (1992)			
	C24	<i>The Comprehensive Sourcebook of Bacterial Protein Toxins</i> , 2 <sup>nd</sup> Ed., Academic Press, pgs. 696-697			
	C25	Tsuji, et al., "Relationship Between a Low Toxicity of the Mutant A Subunit of Enterotoxigenic Escherichia Coli Enterotoxin and its Strong Adjuvant Action." <i>Immunology</i> 90:176-182 (1997)			

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Sheet	3	of	3	Attorney Docket Number	PP000342. 0105 (2300-0342.10)

## OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

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